and pharmaceutically acceptable salts thereof.

35. A pharmaceutical composition comprising a compound selected from the group consisting of

and their pharmaceutically acceptable salts, and a physiologically acceptable carrier.

A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising administering a compound selected from the group consisting

and pharmaceutically acceptable salts thereof.

Please add new claims 37 to 48 as follows:

37. A compound of Formula I:

$$A - D - B$$
 (I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: -L- $(M-L^1)_q$, where L is phenyl bound directly to D, L^1 is phenyl or a 5 to 6 member heteroaryl ring containing 0-4, M is oxygen and q is 1; and

B is a substituted or unsubstituted pyridyl, quinolinyl or isoquinolinyl group,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $-SO_2R_x$, $-C(O)R_x$ and $-C(NR_y)R_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

 R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

 $-OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally



contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

- b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or
- one of R_a or R_b is -C(O)-, a C₁-C₅ divalent alkylene group or a substituted C₁-C₅ divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C₁-C₅ divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L¹ is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R⁷, -C(O)-R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NR⁷R⁷, -NO₂, -NR⁷C(O)R⁷, -NR⁷C(O)OR⁷ and halogen up to per-halo; with each R⁷ independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is a single bond -O-, -S-, -N(R⁷)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-, -(CH₂)_mS-, -(CH₂)_mN(R⁷)-, -O(CH₂)_m- CHX^a-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁷)(CH₂)_m-, wherein m=1-3, and X^a is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1} , wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -NO₂, -OR⁷, -SR⁷ -

 NR^7R^7 , $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, -CO₂R⁷, -COR⁷, -C(O)NR⁷R⁷, -OR⁷, -NO₂, -NR⁷R⁷, -NR⁷C(O)R⁷, and -NR⁷C(O)OR⁷, with R⁷ is defined above.

38. A compound as in claim 37 wherein:

 R_y is hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatoms, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{7-24} aralkyl, C_{7-24} alkaryl, substituted C_{1-10} alkyl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, substituted C_{3-10} cycloalkyl having 0-3 heteroatoms selected from N, S and O, substituted C_{6} - C_{14} aryl, substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C_{7-24} alkaryl or substituted C_{7} - C_{24} aralkyl, where R_y is a substituted group, it is substituted by halogen up to per halo,

 R_z is hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatom, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, C_3 - C_{12} hetaryl having 1-3 heteroatoms selected from S, N and O, C_{7-24} alkaryl, C_{7-24} aralkyl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, substituted C_6 - C_{14} aryl, substituted C_3 - C_{10} cycloalkyl having 0-3 heteroatoms selected from S, N and O, substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from S, N and O, substituted C_{7-24} alkaryl or substituted C_7 - C_{24} aralkyl where R_z is a substituted group, it is substituted by halogen up to per halo, hydroxy, C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_{1-6} halo substituted alkyl up to per halo alkyl, C_6 - C_{12} halo substituted aryl up to per halo aryl, C_3 - C_{12} halo substituted cycloalkyl up to per halo cycloalkyl having 0-3 heteroatoms selected from N, S and O, halo substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from O, N and S, halo substituted C_7 - C_{24} aralkyl up to per halo aralkyl, halo substituted C_7 - C_{24} aralkyl up to per halo aralkyl, halo substituted C_7 - C_{24} alkaryl up to per halo aralkyl, halo substituted C_7 - C_{24} alkaryl up to per halo aralkyl, halo substituted C_7 - C_{24} alkaryl up to per halo aralkyl, halo substituted C_7 - C_{24} alkaryl up to per halo alkaryl, and - $C(O)R_g$,

R_a and R_b are,

a) independently hydrogen,

a carbon based moiety selected from the group consisting of C_1 - C_{10} alkyl, C_1 - C_{10} alkoxy, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, C_{3-12} hetaryl having 1-3 heteroatoms selected from O, N and S, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from N, S and O, C_{7-24} aralkyl, C_7 - C_{24} alkaryl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, substituted C_{3-10} cycloalkyl, having 0-3 heteroatoms selected from N, S and O, substituted C_{6-12} aryl, substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from N. S and O, substituted C_{7-24} aralkyl, substituted C_{7-24} alkaryl, where R_a and R_b are a substituted group, they are substituted by halogen up to per halo, hydroxy, C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_{1-10} halo substituted alkyl up to per halo alkyl, C_6 - C_{12} halo substituted aryl up to per halo aryl, C_3 - C_{12} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_3 - C_{12} hetaryl up to per halo hetaryl, halo substituted C_7 - C_{24} aralkyl up to per halo aralkyl, halo substituted C_7 - C_{24} alkaryl up to per halo alkaryl, and $-C(O)R_g$; or

-OSi(R_f)3 where R_f is hydrogen, C_{1-10} alkyl, C_{1-10} alkyl, C_{1-10} alkoxy, C_3 - C_{10} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{6-12} aryl, C_3 - C_{12} hetaryl having 1-3 heteroatoms selected from O, S and N, C_{7-24} aralkyl, substituted C_{1-10} alkyl, substituted C_1 - C_{10} alkoxy, substituted C_3 - C_{12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, substituted C_3 - C_{12} hetaryl having 1-3 heteroatoms selected from O, S, and N, substituted C_{7-24} alkaryl, where R_f is a substituted group it is substituted halogen up to per halo, hydroxy, C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_{7} - C_{24} alkaryl, C_{7} - C_{24} aralkyl, C_{1-6} halo substituted alkyl up to per halo alkyl, C_6 - C_{12} halo substituted aryl up to per halo aryl, C_3 - C_{12} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_3 - C_{12} hetaryl up to per halo hetaryl, halo substituted C_7 - C_{24} aralkyl up to per halo aralkyl, halo substituted C_7 - C_{24} alkaryl up to per halo hetaryl, halo substituted C_7 - C_{24} aralkyl up to per halo aralkyl, halo substituted C_7 - C_{24} alkaryl up to per halo alkaryl, and - $C(O)R_g$,

or

b) R_a and R_b together from a 5-7 member heterocyclic structure of 1-3 heteroatoms

selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O with substituents selected from the group consisting of halogen up to per halo, hydroxy, C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_7 - C_{24} alkaryl, C_7 - C_{24} aralkyl, halo substituted C_{1-6} alkyl up to per halo alkyl, halo substituted C_6 - C_{12} aryl up to per halo aryl, halo substituted C_3 - C_{12} cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_3 - C_{12} hetaryl up to per halo heteraryl, halo substituted C_7 - C_{12} aralkyl up to per halo aralkyl, halo substituted C_7 - C_{24} alkaryl up to per halo alkaryl, and - $C(O)R_g$,

or

one of R_a or R_b is -C(O)-, a C₁-C₅ divalent alkylene group or a substituted C₁-C₅ divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C₁-C₅ divalent alkylene group are selected from the group consisting of halogen, hydroxy, C₁₋₁₀ alkyl, C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂ hetaryl having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, C₇-C₂₄ alkaryl, C₇-C₂₄ aralkyl, C₁₋₆ halo substituted alkyl up to per halo alkyl, C₆-C₁₂ halo substituted aryl up to per halo aryl, C₃-C₁₂ halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C₃-C₁₂ hetaryl up to per halo heteraryl, halo substituted C₇-C₂₄ aralkyl up to per halo aralkyl, halo substituted C₇-C₂₄ alkaryl up to per halo alkaryl, and -C(O)R_g,

where R_g is C_{1-10} alkyl; -CN, -CO₂R_d, -OR_d, -SR_d, -NO₂, -C(O) R_e, -NR_dR_e, -NR_d C(O)OR_e and -NR_d C(O)R_e, and R_d and R_e are independently selected from the group consisting of hydrogen, C_{1-10} , alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, C_{6-12} aryl, C_3 - C_{12} hetaryl with 1-3 heteroatoms selected from O, N and S and C_7 - C_{24} aralkyl, C_7 - C_{24} alkaryl, up to per halo substituted C_1 - C_{10} alkyl, up to per halo substituted C_3 - C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per halo substituted C_6 - C_{14} aryl, up to per halo substituted C_3 - C_{12} hetaryl having 1-3 heteroatoms selected from O, N, and S, halo substituted C_7 - C_{24} alkaryl up to per halo alkaryl, and up to per halo substituted C_7 - C_{24} aralkyl,



W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R⁷, -C(O)-R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, C₁-c₁₀ alkyl, C₁-C₁₀ alkoxy, C₂-C₁₀ alkenyl, C₁-C₁₀ alkenoyl, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₆-C₁₄ aryl, C₇-C₂₄ alkaryl, C₇-C₂₄ aralkyl, C₃-C₁₂ heteroaryl having 1-3 heteroatoms selected from O, N and S, C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C₁-C₁₀ alkyl, substituted C₁-C₁₀ alkoxy, substituted C₂-C₁₀ alkenyl, substituted C₁-C₁₀ alkenoyl, substituted C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C₆-C₁₂ aryl, substituted C₃-C₁₂ hetaryl having 1-3 heteroatoms selected from O, N and S, substituted C₇-C₂₄ aralkyl, substituted C₇-C₂₄ alkaryl, substituted C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, and -Q-Ar;

 R^7 is independently selected from H, C_1 - C_{10} alkyl, C_1 - C_{10} alkoxy, C_2 - C_{10} alkenyl, C_1 - C_{10} alkenyl, C_3 - C_{10} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_6 - C_{14} aryl, C_3 - C_{13} heteroatoms selected from O, N and S, C_7 - C_{14} alkaryl, C_7 - C_{24} aralkyl, C_4 - C_{23} alkheteroaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C_3 - C_{13} heteroatoms selected from O, N and S, up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl having 0-3 heteroatoms selected form O, N and S, up to per-halosubstituted C_7 - C_{24} aralkyl, up to per-halosubstituted C_7 - C_{24} aralkyl, up to per-halosubstituted C_7 - C_{24} alkaryl, and up to per-halosubstituted C_4 - C_{23} alkheteroaryl; and

each Z is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -NO₂, -OR⁷, -SR⁷ -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, C₁-c₁₀ alkyl, C₁-C₁₀ alkoxy, C₂-C₁₀ alkenyl, C₁-C₁₀ alkenoyl, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, C₆-C₁₄ aryl, C₃-C₁₃ hetaryl having 1-3 heteroatoms selected from O, N and S, C₇-C₂₄ alkaryl, C₇-C₂₄ aralkyl, C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C₁-C₁₀ alkyl, substituted C₁-C₁₀ alkoxy, substituted C₂-C₁₀ alkenyl, substituted C₁-C₁₀ alkenyl, substituted C₁-C₁₀ alkenyl, substituted C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C₆-C₁₂ aryl, substituted C₇-C₂₄ alkaryl, substituted C₇-C₂₄ aralkyl and substituted C₄-

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 C_{23} alkheteroaryl having 1-3 heteroatoms selected from O, N and S; wherein if Z is a substituted group, the one or more substituents are selected from the group consisting of -CN, -CO₂R⁷, -CO₂R⁷, -CO₂NR⁷R⁷, -OR⁷, -NO₂, -NR⁷R⁷, -NR⁷C(O)R⁷, and -NR⁷C(O)OR⁷.

- 39. A compound as in claim <u>37</u> wherein the cyclic structures of B and L bound directly to D are not substituted in the ortho position by -OH.
- 40. A compound of claim 37 wherein B of Formula I is a substituted pyridyl, substituted quinolinyl or isoquinolinyl group substituted 1 to 3 times by 1 or more substituents selected from the group consisting of -CN, halogen, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, -OH, up to per halo substituted C₁-C₁₀ alkyl, up to per halo substituted C₁-C₁₀ alkoxy or phenyl substituted by halogen up to per halo.
- 41. A compound of claim <u>37</u>, wherein said substituted cyclic moiety L¹ is phenyl, pyridinyl or pyrimidinyl.
- 42. A compound of claim 37 wherein L¹ is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C₁-C₁₀ alkyl, up to per halo substituted C₁-C₁₀ alkyl, -CN, -OH, halogen, C₁-C₁₀ alkoxy and up to per halo substituted C₁-C₁₀ alkoxy.
- 43. A compound of claim 1 wherein L^1 is substituted by $-C(O)R_x$ or $-SO_2R_x$, wherein R_x is NR_aR_b .
- 44. A compound of claim 37 wherein L^1 is substituted by $-C(O)R_x$, wherein R_x is NR_aR_b and R_a and R_a are independently hydrogen or a carbon based moiety of up to 30 carbon

atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

- 45. A compound as in claim 37 wherein substituents for B and L and additional substituents for L¹, are selected from the group consisting of C₁-C₁₀ alkyl up to per halo substituted C₁-C₁₀ alkyl, CN, OH, halogen, C₁-C₁₀ alkoxy and up to per halo substituent C₁-C₁₀ alkoxy.
- 46. A compound of claim 37 which is a pharmaceutically acceptable salt of a compound of formula I selected from the group consisting of
 - a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluorosulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and
 - b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.
- 47. A pharmaceutical composition comprising a compound of claim 37 or a pharmaceutically acceptable salt of a compound of formula I, and a physiologically acceptable carrier.
- 48. A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising administering a compound of Formula I of claim 37.